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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/512,363	02/23/00	NI J	PF396P1

022195
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HM12/1023

EXAMINER	
HOLLERAN, A	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/512,363	Applicant(s) NI ET AL.	
	Examiner Anne Holleran	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed August 13, 2001 (Paper No. 10) is acknowledged.

Claims 1-47 are pending.

Election/Restrictions

2. Applicant's election with traverse of claims 19-46 (originally referred to as 19-47 because of an error in claim numbering) in Paper No. 9, filed June 4, 2001 is acknowledged. The traversal is on the ground(s) that there is no serious burden imposed upon the examiner to examine all of the invention groups. This is not found persuasive because a prima facie case for burden of examination is made when the examiner demonstrates that the different invention groups different classifications, and would require different searches. As applicant has failed to specifically point out any error in restriction requirement, the restriction requirement is maintained.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-18, and 47, drawn to non-elected inventions, are withdrawn from consideration.

Claims 1-46 are examined on the merits.

Sequence Listing

4. In processing the CRF copy of the sequence listing, the STIC removed non-ASCII "garbage" at the end of the file.

Priority

5. Applicant's claim for priority under 35 U.S.C. 120 and 119(e) is acknowledged. However, the continuation-in-part parent application (09/176,200) upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claim 19-46 of this application. Application 09/176,200 fails to provide written description of methods drawn to inhibiting the binding of Endokine-alpha to an endogenous Endokine-alpha receptor. Furthermore, application 09/176,200 fails to provide support for fragments of SEQ ID NO: 2 as recited in claims 19 and 33.

Claim Rejections - 35 USC § 112

6. Claims 19-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19-46 are indefinite because it is not clear how claims 19 and 33 (each independent claims, from which claims 20-32 and 34-46, respectively, depend) differ in scope. The specification teaches that the polynucleotide encoded by the cDNA clone deposited as ATCC 209341 encodes a polypeptide that has the amino acid sequence of SEQ ID NO: 2. Thus, claims 19 and 33 appear to be drawn to inventions of the same scope.

7. Claims 19-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The basis for this rejection is two-fold. First, newly added claims 19-46 appear to introduce new matter into the specification as originally filed, because newly added claims 19-46 are drawn to methods using fragments of SEQ ID NO: 2 that are not described in the specification. Thus, it appears that claims 19-46 are drawn to methods that were not contemplated at the time of filing. Secondly, claims 19-46 are drawn to methods using TR11 polypeptides identified in the claims as polypeptides comprising fragments of SEQ ID NO: 2 or fragments of a polypeptide sequence encoded by a deposited cDNA clone. Thus, claims 19-46 are drawn to methods using a genus of polypeptide molecules, the species of which vary widely in structure, and for which the structure of SEQ ID NO: 2 does not appear to be a representative amino acid sequence.

A. The methods of claims 19-46 may be interpreted as methods using specific fragments of SEQ ID NO: 2. Applicant points to several passages in the specification as passages that support the subject matter of newly added claims 19-46. However, the passages do not provide literal support for claims drawn to methods using fragments of SEQ ID NO: 2 as recited in subsections "c" through "i" of claims 19 or 33. The specification appears to provide support for subsections "a" and "b" (found on page 49, line 31 and page 59, line 3). Because subsections "c" through "i" of claims 19 and 33 are drawn to specifically defined fragments of SEQ ID NO: 2, or of a polypeptide encoded by a deposited cDNA clone, the specification or the claims as originally presented must teach or recite these fragments as evidence that the methods as claimed were

contemplated at the time the invention was filed. Merely teaching the amino acid sequence of SEQ ID NO: 2 or the generic concept of fragments of SEQ ID NO: 2 is not adequate to allow one of skill in the art to readily envisage the specific fragments recited in subsections "c" through "i" of claims 19 and 33. Thus, it does not appear that the claimed inventions were in the possession of the inventors at the time the application was filed.

B. Claims 19-46 are drawn to methods using a genus of TR11 polypeptides, the species of which vary widely in structure, and for which the structure of SEQ ID NO: 2 does not appear to be a representative amino acid sequence. The TR11 polypeptides of claims 19 through 46 vary widely in structure because claims 19 and 33 recite open language when describing the different peptide structures of subsections "a" through "i" of claims 19 and 33. Any sequence may be added to either end of the recited fragments to make a species of TR11 polypeptide. The specification teaches only one example of a TR11 polypeptide, a polypeptide whose amino acid sequence is the amino acid sequence of SEQ ID NO: 2. The specification fails to describe a genus of TR11 polypeptides that encompasses amino acid sequences other than the amino acid sequence of SEQ ID NO: 2. Thus, the broadly claimed methods, using TR11 polypeptides whose structures are not fully recited in the claims, and have not been taught in the specification, are not supported by the specification, and one of skill in the art would not find that applicant was in possession of methods of inhibiting the binding of Endokine alpha using the TR11 polypeptides as recited in claims 19 and 33.

8. Claims 19-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation would be required to make and use the invention or to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

Claims 19-46 are drawn to methods of inhibiting the binding of Endokine alpha to endogenous Endokine alpha receptors comprising administering a TR11 polypeptide. The structures of the TR11 polypeptides to be used in the claimed methods are not completely recited in the claims. Claims 32 and 46 add the limitation that the TR11 polypeptide inhibits migration of T-cells across endothelial cells. However, the specification fails to teach that such a TR11 polypeptide has been discovered and fails to teach a structure of an example of such a TR11 polypeptide. The scope of the claimed methods is broad because the claimed methods may use any species of TR11 polypeptide derived from an incompletely characterized genus of polypeptides.

The specification provides data to demonstrate that a polypeptide having the amino acid sequence of SEQ ID NO: 2 binds to soluble Endokine alpha. Thus, from this example, it appears

that a polypeptide with the amino acid sequence of SEQ ID NO: 2 may be used to inhibit the binding of Endokine alpha to an Endokine alpha receptor. The specification fails to identify a region of SEQ ID NO: 2 that is critical for binding with soluble Endokine alpha. Thus, the specification fails to enable methods using TR11 polypeptides that do not have the same sequence as SEQ ID NO: 2. It is well known that protein structure and function relationships are unpredictable and that small changes in the primary amino acid sequence may result in loss of function of a protein or in a different function of a protein. Lazar et al teaches that a change of 1 amino acid residue results in different biological activities of TGF-α, and Burgess teaches that a change in a single lysine residue results in loss of function of Heparin-binding Growth Factor-1 (see Lazar, E. et al. Mol. Cell. Biol., 8: 1247-1252, 1988; Burgess, W.H. et al., J. Cell Biology, 111: 2129-2138, 1990). Because of the breadth of the claims with respect to the widely varying amino acid structures and because of the unpredictability of protein chemistry with respect to function of proteins, the specification, by only teaching one example and failing to teach a region of SEQ ID NO: 2 that is critical for binding with soluble Endokine alpha, one of skill in the art would have to engage in undue experimentation to make the inventions as claimed.

Additionally, the specification fails to teach how to use the claimed methods for any specific purpose. Because the methods are drawn to methods comprising administering to a mammal TR11 polypeptides, it appears that the claimed methods read on methods of treatment. It is not clear from the specification why one would want treat a mammal by inhibiting the binding of Endokine alpha to endogenous Endokine alpha receptors. The specification fails to teach the identity of endogenous Endokine alpha receptors. There does not appear to be evidence in the art or in the specification that Endokine alpha receptors are associated with a

disease state. The specification teaches that binding of a polypeptide having the amino acid sequence of SEQ ID NO: 2 with soluble Endokine alpha results in activation of NF-kappaB, which is a transcription factor. However, NF-kappaB is a transcription factor that regulates a multitude of genes. Furthermore, the specification fails to teach that binding of Endokine alpha with an endogenous Endokine alpha receptor activates NF-kappaB. Therefore, the specification presents an invitation to experiment, first to discover whether binding of Endokine alpha with its endogenous receptor is associated with a disease state, and second to discover which species of the many encompassed by the genus "TR11 polypeptide" may be useful in the claimed methods. Thus, one of skill in the art would have to engage in undue experimentation to learn how to use the claimed inventions and to know how to make the full scope of the claimed inventions.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 19- 21, 26, 27, 33-35, 40 and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Gorman et al[a] (U.S. Patent 6,111,090; issued Aug. 29, 2000; effective filing date Aug. 16, 1996).

Claims 19 and 33 are drawn to methods of treatment comprising administering to a mammal a TR11 polypeptide where the polypeptide comprises various fragments of SEQ ID NO: 2. The fragments may be amino acid residues –25 – 137; 1-137; 1-114; -25-139; 21-139; 8-129; 8-48; 49-88 and 88-129; where the TR11 polypeptide is in a pharmaceutically acceptable carrier. Claims 20 and 34 are drawn to methods where the mammal is a human; claims 21 and 35 are drawn to methods where the TR-11 polypeptide is fused to a heterologous polypeptide. Claims 26, 27, 40 and 41 are drawn to methods where the pharmaceutical carrier is water or saline.

Gorman[a] teaches methods of treatment comprising administering 312C2 polypeptides in pharmaceutical carriers (see col. 3, lines 16-19; col. 21, lines 36-52; col. 23, lines 9-52), which are polypeptides that comprise the fragments recited in claims 19 and 33 (see enclose sequence alignments). Gorman[a] also teaches fusion peptides (see col. 13, line 64-col. 14, line 2). Gorman[a] teaches the human form of 312C2 polypeptides (col. 10, lines 44-46). Thus, Gorman[a] teaches methods that are the same as that claimed.

10. Claims 19- 21, 26, 27, 33-35, 40 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorman et al[b] (WO 98/06842; published 19 February 1998).

Applicant's claim to priority to copending application 09/176,200 (continuation-in-part parent) is denied because application 09/176,200 fails to disclose the invention as claimed. Thus, the effective filing date with respect to the prior art is the filing date of the instant application.

Gorman[b] teaches 312C2 polypeptides in pharmaceutical carriers (page 4; page 35- page 36; page 38-39). Gorman[b] also teaches fusion peptides (page 23). Gorman[b] also teaches the human form of 312C2 polypeptides (page 17). Thus, Gorman[b] teaches methods that are the same as that claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 19, 21-24, 33, 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Gorman[a] or Gorman[b] in view of Capon et al (U.S. Patent 5,116,964; issued May 26, 1992).

Claims 21-24 and 35-38 are drawn to methods where the TR-11 polypeptide is a fusion polypeptide where the heterologous polypeptide is an immunoglobulin constant domain; where the immunoglobulin constant domain may be an IgG1 constant domain or an IgG3 constant domain.

Gorman[a] or Gorman[b] teaches methods of treatment comprising administering fusion polypeptides, but fails to teach methods of treatment where the heterologous polypeptide is an immunoglobulin constant domain. However, the use, in methods of treatment, of fusion polypeptides comprising immunoglobulin fusion domains is known in the art as evidenced by the

teachings of Capon. Capon teaches that fusion of a therapeutic protein to an immunoglobulin constant domain is useful because such fusion proteins are more stable in serum and because fusion with an immunoglobulin constant domain adds the functionality of immunoglobulin effector functions such as complement binding (col. 4, lines 16-47). Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Gorman[a] or Gorman[b] by making fusion proteins where the heterologous protein was an immunoglobulin fusion protein such as IgG1 or IgG3 as taught by Capon.

13. Claims 19, 21, 25, 33, 35, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Gorman[a] or Gorman[b] in view of Sivam et al (U.S. Patent 5,116,944; issued 5/26/1992).

Claims 25 and 39 are drawn to methods comprising administering TR11 fusion polypeptides where the heterologous polypeptide is human serum albumin.

Gorman[a] or Gorman[b] teaches methods of treatment comprising administering fusion polypeptides, but fails to teach methods of treatment where the heterologous polypeptide is human serum albumin. However, the use of human serum albumin in human therapeutic formulations is well known in the art as evidenced by the teachings of Sivam. Sivam teaches that human serum albumin is known in the art as a drug carrier intermediate, as a targeting agent and as a stabilizing agent (col.3, lines 5-29). Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods

of Gorman[a] or Gorman[b] by making fusion proteins where the heterologous protein was human serum albumin because of the uses of human serum albumin as taught by Sivam.

14. Claims 19, 28-31, 33, and 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Gorman[a] or Gorman[b].

Claims 28-31 and 42-45 are drawn to methods where the pharmaceutical carrier is either Ringer's solution, dextrose solution, ethyl oleate or is a liposome. Gorman[a] and Gorman[b] teach methods of administering polypeptides in pharmaceutically acceptable carriers, but fail to list Ringer's solution, dextrose solution, ethyl oleate or liposomes. However, each of these carriers is an art-known carrier, and one of ordinary skill in the art would be able to use each of these carriers with the polypeptides of Gorman[a] or Gorman[b]. Furthermore, Gorman[a] and Gorman[b] teaches that pharmaceutical carriers other than the ones listed in the references may be found by consulting various pharmacology text books. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used any of the carriers of claims 28-31 or claims 42-45.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

ALH

Anne L. Holleran
Patent Examiner
October 20, 2001

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